

## PARENT COOPERATION TREATY

PCT

NOTIFICATION CONCERNING  
SUBMISSION OR TRANSMITTAL  
OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

From the INTERNATIONAL BUREAU

To:

TABUSHI, Eiji  
Fujisawa Pharmaceutical Co., Ltd.  
Osaka Factory  
1-6, Kashima 2-chome  
Yodogawa-ku, Osaka-shi  
Osaka 532-8514  
JAPON

Date of mailing (day/month/year) 26 January 2000 (26.01.00)	<b>IMPORTANT NOTIFICATION</b>
Applicant's or agent's file reference PWO-19174	
International application No. PCT/JP00/00018	
International publication date (day/month/year) Not yet published	
International filing date (day/month/year) 06 January 2000 (06.01.00)	Priority date (day/month/year) 07 January 1999 (07.01.99)
Applicant FUJISAWA PHARMACEUTICAL CO., LTD. et al	

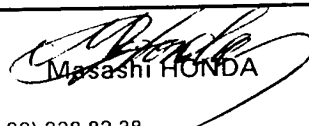
- The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
- An **asterisk(\*)** appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- The **letters "NR"** appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

<u>Priority date</u>	<u>Priority application No.</u>	<u>Country or regional Office or PCT receiving Office</u>	<u>Date of receipt of priority document</u>
07 Janu 1999 (07.01.99)	PP8068	AU	21 Janu 2000 (21.01.00)
19 July 1999 (19.07.99)	PQ1702	AU	21 Janu 2000 (21.01.00)

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

  
Masashi HONDA

Telephone No. (41-22) 338.83.38

PCT

NOTICE INFORMING THE APPLICANT OF THE  
COMMUNICATION OF THE INTERNATIONAL  
APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

From the INTERNATIONAL BUREAU

To:

TABUSHI, Eiji  
Fujisawa Pharmaceutical Co., Ltd.  
Osaka Factory  
1-6, Kashima 2-chome  
Yodogawa-ku, Osaka-shi  
Osaka 532-8514  
JAPON

Date of mailing (day/month/year) 13 July 2000 (13.07.00)		
Applicant's or agent's file reference PWO-19174		IMPORTANT NOTICE
International application No. PCT/JP00/00018	International filing date (day/month/year) 06 January 2000 (06.01.00)	Priority date (day/month/year) 07 January 1999 (07.01.99)
Applicant FUJISAWA PHARMACEUTICAL CO., LTD. et al		

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:

AU,CN,JP,KR,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AE,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,CA,CH,CU,CZ,DE,DK,EA,EE,EP,ES,FI,GB,GD,GE,GH,GM,  
HR,HU,ID,IL,IN,IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MN,MW,MX,NO,NZ,OA,PL,PT,  
RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,UA,UG,UZ,VN,YU,ZA,ZW

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on  
13 July 2000 (13.07.00) under No. WO 00/40576

## REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a **demand for international preliminary examination** must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

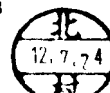
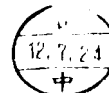
Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

## REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the **national phase**, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer  J. Zahra
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38



# PATENT COOPERATION TREATY

PCT/JP00/00018

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C. 20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 24 August 2000 (24.08.00)	
<b>International application No.</b> PCT/JP00/00018	<b>Applicant's or agent's file reference</b> PWO-19174
<b>International filing date</b> (day/month/year) 06 January 2000 (06.01.00)	<b>Priority date</b> (day/month/year) 07 January 1999 (07.01.99)
<b>Applicant</b> TANIGUCHI, Kiyoshi et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
21 July 2000 (21.07.00)

☐ in a notice effecting later election filed with the International Bureau on:  
\_\_\_\_\_

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<b>The International Bureau of WIPO</b> 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	<b>Authorized officer</b> Christelle Croci Telephone No.: (41-22) 338.83.38
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(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
13 July 2000 (13.07.2000)

PCT

(10) International Publication Number  
**WO 00/40576 A3**

(51) International Patent Classification<sup>7</sup>: C07D 335/02,  
A61K 31/38, 31/385, 31/44, C07D 339/08, 333/48,  
409/04, 409/12, 409/14, A61P 29/00, 31/18

(21) International Application Number: PCT/JP00/00018

(22) International Filing Date: 6 January 2000 (06.01.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
PP 8068 7 January 1999 (07.01.1999) AU  
PQ 1702 19 July 1999 (19.07.1999) AU

(71) Applicant (for all designated States except US): FUJISAWA PHARMACEUTICAL CO., LTD. [JP/JP]; 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP).

(72) Inventors; and

(75) Inventors/Applicants (for US only): TANIGUCHI, Kiyoshi [JP/JP]; 2-1-28, Minamiochiai, Suma-ku, Kobe-shi, Hyogo 654-0153 (JP). NEYA, Masahiro [JP/JP]; 4016-25, Hitana, Tsuchiura-shi, Ibaraki 300-0065 (JP). TERASAWA, Takeshi [JP/JP]; 3-10-11, Ibukino, Izumi-shi, Osaka 594-0041 (JP). YAMAZAKI, Hitoshi [JP/JP]; 4-3-4, Matsushiro, Tsukuba-shi, Ibaraki 305-0035 (JP). SATO, Kentaro [JP/JP]; 2-25-10-202, Matsushiro, Tsukuba-shi, Ibaraki 305-0035 (JP). HOSOI, Kumi [JP/JP]; 91-2-A-305, Futatsuya, Susono-shi, Shizuoka, 410-1128 (JP). TOMISHIMA, Yasuyo [JP/JP]; 5-5-24-706, Toyosaki, Kita-ku, Osaka-shi, Osaka 531-0072 (JP). YOSHIDA, Noriko [JP/JP]; 2-23-4-408,

Matsushiro, Tsukuba-shi, Ibaraki 305-0035 (JP). IMA-MURA, Yoshimasa [JP/JP]; 2-25-10-208, Matsushiro, Tsukuba-shi, Ibaraki 305-0035 (JP). TAKASUGI, Hisashi [JP/JP]; 3-116-10, Mozu Umekita, Sakai-shi, Osaka 591-8031 (JP). SETOI, Hiroyuki [JP/JP]; 4-13-1, Namiki, Tsukuba-shi, Ibaraki 305-0044 (JP).

(74) Agent: TABUSHI, Eiji; Fujisawa Pharmaceutical Co., Ltd., Osaka Factory, 1-6, Kashima 2-chome, Yodogawa-ku, Osaka-shi, Osaka 532-8514 (JP).

(81) Designated States (national): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

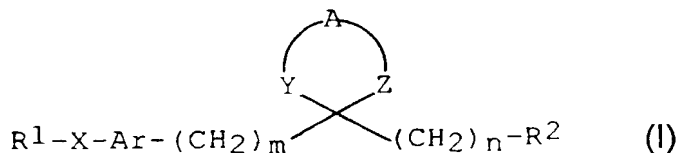
Published:

— With international search report.

(88) Date of publication of the international search report:  
22 March 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: THIOPYRAN COMPOUNDS AS INHIBITORS OF MMP



(57) Abstract: A compound of formula (I) in which R<sup>1</sup> is lower alkyl, halogen, optionally substituted heterocyclic group or optionally substituted aryl, R<sup>2</sup> is carboxy, protected carboxy or amidated carboxy, Ar is optionally substituted aryl or optionally substituted heterocyclic group, A is lower alkylene, X is oxa or a single bond, Y is thia, sulfinyl or sulfonyl, Z is methylene, thia, sulfinyl or sulfonyl, m and n are each an integer

of 0 to 6, and 1 ≤ m + n ≤ 6, or its salt, which is useful as an inhibitor of matrix metalloproteinases (MMP) or tumor necrosis factor α (TNF α).

WO 00/40576 A3

# INTERNATIONAL SEARCH REPORT

International Application No.

PCT/JP 00/00018

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D335/02 A61K31/38 A61K31/385 A61K31/44 C07D339/08  
C07D333/48 C07D409/04 C07D409/12 C07D409/14 A61P29/00  
A61P31/18

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	I. STAHL ET AL.: "2,2-DISUBSTITUIERTE 1,3-DITHIANE" CHEMISCHE BERICHTE., vol. 113, no. 2, 1980, pages 800-5, XP002151298 VERLAG CHEMIE GMBH. WEINHEIM., DE ISSN: 0009-2940 page 800 -page 804; examples 6,7,13,14 ---	1
A	EP 0 326 297 A (MAY & BAKER) 2 August 1989 (1989-08-02) page 1 -page 14 -----	1,11,12

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

27 October 2000

Date of mailing of the international search report

10/11/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo.nl,  
Fax: (+31-70) 340-3016

Authorized officer

Francois, J

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/JP 00/00018

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claim 16 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

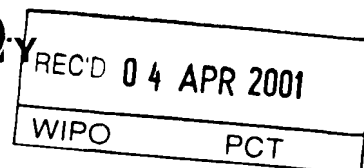
# INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/JP 00/00018

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 326297	A	02-08-1989	AT 73795 T	15-04-1992
			CA 1335672 A	23-05-1995
			DE 68900990 D	23-04-1992
			DK 23089 A	22-07-1989
			ES 2033523 T	16-03-1993
			FI 890293 A	22-07-1989
			GR 3004363 T	31-03-1993
			HU 49340 A,B	28-09-1989
			JP 1308275 A	12-12-1989
			NZ 227682 A	26-02-1991
			OA 9032 A	31-03-1991
			PT 89492 A,B	04-10-1989
			US 4959385 A	25-09-1990
			ZA 8900479 A	25-10-1989



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference PWO-19174	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/JP00/00018	International filing date (day/month/year) 06/01/2000	Priority date (day/month/year) 07/01/1999
International Patent Classification (IPC) or national classification and IPC C07D335/02		
Applicant FUJISAWA PHARMACEUTICAL CO., LTD. et al.		

- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 6 sheets, including this cover sheet.
  - ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

- This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  21/07/2000	Date of completion of this report  30.03.2001
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Grassi, D  Telephone No. +49 89 2399 8499  



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/JP00/00018

**I. Basis of the report**

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):*

**Description, pages:**

1-294 as originally filed

**Claims, No.:**

1-17 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
  - ☐ the language of publication of the international application (under Rule 48.3(b)).
  - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
  - ☐ filed together with the international application in computer readable form.
  - ☐ furnished subsequently to this Authority in written form.
  - ☐ furnished subsequently to this Authority in computer readable form.
  - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
4. The amendments have resulted in the cancellation of:
- ☐ the description, pages:
  - ☐ the claims, Nos.:
  - ☐ the drawings, sheets:
5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/JP00/00018

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 13,14,16,17 (with respect to industrial applicability).

because:

- ☒ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .
2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes:	Claims 6-17
	No:	Claims 1-5
Inventive step (IS)	Yes:	Claims
	No:	Claims 1-17
Industrial applicability (IA)	Yes:	Claims 1-12,15

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/JP00/00018

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No: Claims

2. Citations and explanations  
**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/JP00/00018

**Re Item III**

Claims 13, 14, 16 and 17 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

**Re Item V**

- 1) Reference is made to the following documents:  
D1: I. STAHL ET AL.: '2,2-DISUBSTITUIERTE 1.3-DITHIANE' CHEMISCHE BERICHTE., vol. 113, no. 2, 1980, pages 800-5, XP002151298 VERLAG CHEMIE GMBH. WEINHEIM., DE ISSN: 0009-2940  
D2: US-A-5 747 514 (a copy is attached)
- 2) The subject-matter of present claims 1-5 is not new (Article 33(2) PCT).  
The compounds **3e, f** and **11c, d** of D1 fall within the terms of the said claims.
- 3) The novel part of claims 1-4 and the claims 6-9 do not involve an inventive step (Article 33(3) PCT).

D2 discloses compounds inhibiting metalloproteinases and the release of tumor necrosis factor (cf. abstract).

The problem underlying the present application is seen in the provision of alternative compounds exhibiting said properties.

The present description shows that one compound (example 15) exhibits the alleged activity.

Having regard to the very broad terms of the present claims it is not credible that essentially all of the claimed compounds solve the technical problem (A contains 2 to 6 carbon atoms, R<sup>1</sup> encompasses any heterocyclic group with no limitation to ring size or substituents, Ar encompasses any aromatic group with no limitation to ring size or substituents, R<sup>1</sup> encompasses any carboxy or amid residue).

The applicant is therefore requested to submit further test data supporting the

breath of the present claims or to restrict the claims to a group of compounds for which the alleged activity is credible.

- 4) The claims 10-17 would only be regarded as involving inventive activity if the claim 1 fulfilled said requirement.
- 5) For the time being, the **novel part** of claim 5 is regarded as inventive. In view of the active compound of example 15, it is credible that the group of compounds according to claim 5 exhibits similar properties and therefore solve the technical problem.
- 6) For the assessment of the present claims 11-17 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

#### **Re Item VIII**

- 1) The invention appears not to be sufficiently disclosed (Art. 5 PCT).  
Compounds according to the present claims 1-5 in which X is oxa, R<sup>1</sup> is halogen and Y/Z are thia appear not to be stable. The description does not enable the skilled person prepare such compounds.
- 2) The present claims are not clear (Art. 6 PCT).
  - 2.1) The term "lower" is not clear.
  - 2.2) The term "lower alkenyl" in connection with fragment A is not clear.
  - 2.3) The claim 7 contains an error. It appears that R<sup>1</sup> (cf. page 309, line 31) should be replaced by R<sup>11</sup>.

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>PWO-19174</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/JP 00/00018</b>	International filing date (day/month/year) <b>06/01/2000</b>	(Earliest) Priority Date (day/month/year) <b>07/01/1999</b>
Applicant <b>FUJISAWA PHARMACEUTICAL CO., LTD. et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of **3** sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

### 1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

**THIOPYRAN COMPOUNDS AS INHIBITORS OF MMP**

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.